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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,009	11/08/1999	CAROL MORRIS	047763-5010	3768

9629 7590 11/06/2002

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/06/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/367,009	MORRIS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 6-12* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claim 5.

Accordingly, claims 1, 3, 6-11 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

Claims 1, 3, 6-9 are indefinite, because claims 1 and 3 are missing an important step of how to analyze or detect in a tear sample from an animal the presence of a protein having a N-terminal amino acid sequence comprising SEQ ID NO:3.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 1, 3, 6-11 are rejected under 112, first paragraph.

Claims 1, 3, 6-9 are drawn to a method of screening for or detecting cancer in an animal, comprising obtaining and analyzing or detecting in a tear sample from the animal for the presence of a protein having a N-terminal amino acid sequence "comprising" SEQ ID NO:3, using labeled "probes specific" for a protein having a N-terminal amino acid sequence "comprising" SEQ ID NO:3.

Claims 10-11 are drawn to a protein detectable in tears "comprising" SEQ ID NO:3 or havig a N-terminal amino acid sequence "comprising" SEQ ID NO:3.

The specification, the response and the COBON Declaration of 03/14/02 disclose that the claimed detection of various cancers is done by detecting the frequency of expression of a spot on 2D-PAGE of a tear sample, wherein said spot has a MW of 10 KD and a pI of 5.1 (table 2 on page 7 of the specification, and the annexed table C in the Declaration). The specification also discloses that partial sequencing of the protein isolated from said spot show a sequence of SEQ ID NO:3 (p.7).

It is noted that SEQ ID NO:3 is a fragment of the claimed protein. It is further noted that the claims 1, 3, 6-9 as written encompass a method of screening for or detecting cancer in an animal, comprising obtaining and analyzing or detecting in a tear sample from the animal for the presence of unrelated proteins which share with the claimed protein the polypeptide fragment of SEQ ID NO:3. Claims 10-11 encompass unrelated proteins which share with the claimed protein the polypeptide fragment of SEQ ID NO:3. Further, due to the language "using labeled "probes specific" for a protein having a N-terminal amino acid sequence comprising SEQ ID NO:3", the claims

encompass a method for detecting cancer, using antibodies against specific epitopes of unrelated proteins sharing with the claimed protein a N-terminal amino acid sequence comprising SEQ ID NO:3. The structure of the epitopes specific for the claimed protein however is not disclosed in the specification.

Although drawn specifically to the DNA art, the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly relevant to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The instant disclosure of a single species of a protein does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length proteins. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no

information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed and no identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific peptide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Thus, only a method of screening for or detecting cancer in an animal, comprising obtaining and analyzing or detecting in a tear sample from the animal for the presence of the amino acid sequence consisting of SEQ ID NO:3, and the amino acid sequence consisting of SEQ ID NO:3, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

If Applicant could overcome the above 112, first paragraph rejections, claims 1,3, 6-9 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting cancer, comprising detecting in a tear

sample the presence of SEQ ID NO:3 from a protein having a MW of 10KD and a pI of 5.1, the N-terminal amino acid sequence thereof consists of SEQ ID NO:3, using labeled probes specific for SEQ ID NO:3, does not reasonably provide enablement for a method of screening for or detecting cancer in an animal, comprising obtaining and analyzing or detecting in a tear sample from the animal for the presence of a protein having N-terminal amino acid sequence comprising SEQ ID NO:3, using labeled "probes specific" for a protein having a N-terminal amino acid sequence comprising SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims 1, 3, 6-9 are drawn to a method of screening for or detecting cancer in an animal, comprising obtaining and analyzing or detecting in a tear sample from the animal for the presence of a protein having N-terminal amino acid sequence comprising SEQ ID NO:3, using labeled "probes specific" for a protein having a N-terminal amino acid sequence comprising SEQ ID NO:3.

The specification, the response and the COBON Declaration of 03/14/02 of disclose that the detection of breast, lung, colon and prostate cancer is done by detecting the frequency of expression of a spot on 2D-PAGE of a tear sample, wherein said spot has a MW of 10 KD and a pI of 5.1, and wherein cancer patients have higher frequency of the presence of said spot in a tear sample (table 2 on page 7 of the specification, and the annexed table C in the Declaration). The specification also

discloses that partial sequencing of the protein isolated from said spot show a sequence of SEQ ID NO:3 (p.7 of the specification).

One cannot extrapolate the teaching of the specification to the scope of the claims. The claims as written encompass a method for detecting cancer, using antibodies against specific epitopes of unrelated proteins in a tear sample which share with the claimed protein a N-terminal amino acid sequence comprising SEQ ID NO:3. The structure of the epitopes specific for the claimed protein however is not disclosed in the specification. There is no teaching in the specification of whether or not the epitopes are linear or comprise 3-dimensional structures. Herbert et al. (The Dictionary of Immunology, Academic Press, 4th edition, 1995, p.58) define epitopes as the region on an antigen molecule to which antibody or the T cell receptor binds specifically wherein the 3-dimensional structure of the protein molecule may be essential for antibody binding. However, the specification fails to disclose sufficient guidance and objective evidence as to the linear and or three-dimensional conformation of the polypeptide fragments which constitute epitopes recognized by the claimed invention. Antibodies bind to structural shapes that may be linear stretches of amino acids, conformational determinants formed by the folding of peptides, carbohydrate moieties, phosphate or lipid residues or a combination thereof. Moreover, as evidenced by Greenspan et al, defining epitopes is not as easy as it seems (Nature Biotechnology 7:936-937 (1999). Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column).

Further, without disclosure of specific epitopes of the claimed antibodies, antibodies that bind specifically or selectively for SEQ ID NO:5 would also detect unrelated proteins, because an antibody could be specific or selective for only one or two amino acids epitopes, wherein said one or two amino acids could be shared by unrelated proteins. Moreover, although it is routine in the art how to make antibodies, the antibody epitopes that are specific for a protein are not predictable. Thus, since the specification has not identified which amino acids and or polypeptide fragments are critical or essential characteristics of the epitope, one of skill in the art would not know how the use the claimed method.

For the above reasons, undue experimentation would be required to enable the claims as written.

REJECTION UNDER 35 USC 102

Rejection under 35 USC 102(a) of claims 1, 3, 6-8, 10-11 pertaining to anticipation by Molloy et al remains for reasons already of record in paper No.15.

Applicant argues that the parent Australian application PO5009 has a priority date of Feb 7/97, while Molloy et al has a publication date of December 18, 1997. Applicant further asserts that Applicant is willing to provide a certified copy of the priority application, which is in the application PCT/AU98/00071, in the event that said copy is not available.

Applicant's arguments set forth in paper No.16 have been considered but are not deemed to be persuasive for the following reasons:

Rejection remains because a certified copy of the priority application is not available.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

October 27, 2002